(ns vs 0). *Conclusion:* 3D reconstruction can improve spatial appreciation of the shape of thrombi and accurately measure their volumes. This approach, suitable for epivascular or transvenous imaging, could potentially be used to study thrombus formation and lysis in research and clinical studies.

PHARMACOLOGY — BASIC

901-111 ACE Inhibition (Quinapril) Modulates Central Vasopressin in the Rat

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The beneficial effects of ACE inhibitors (ACEI) in heart failure and hypertension appear to be mediated not only by their influence on circulating ACE or tissue ACE in the heart. Previous studies have also implicated the brain as a possible site of actions for ACEI, e.g. by modifying central cardiovascular mechanisms. Their effects on central vasopressin (AVP), which is an important neurotransmitter in central cardiovascular regulation, are not known.

Following chronic administration of Quinapril (6 mg/kgBW; 6 weeks, p.o.) ACE activity (in vitro autoradiography using a specific ACE inhibitor [^{125}I]351A) was markedly inhibited in the thalamus (38%), hypothalamus (37%), hypophysis (35%), cerebellum (36%) and plexus choroideus (20%) suggesting Quinapril may cross the blood brain barrier after chronic treatment. To study the influence of ACEI on central vasopressin, we determined the AVP content of 19 microdissected brain areas in rats treated with Quinapril. Regarding the hypothalamic AVP-producing nuclei, increased AVP levels could only been demonstrated in the paraventricular (PVN; Quinapril: 292 ± 197 vs. 2209 ± 568 pg/mg protein of controls; $p < 0.001$), but not in the supraoptic (SON) and the suprachiasmatic nucleus (SCN). Interestingly, vasopressin synthesizing cells in the PVN project not only to the posterior pituitary (like SON), but also to the lower brain stem and the spinal cord suggesting an important role of the PVN in the regulation of the cardiovascular system. Also, AVP content was sign. reduced in the median eminence (15643 ± 9240 vs. 28321 ± 4969, $p < 0.001$), where the hormone is mainly concentrated in the hypothalamo-hypophysial tract. Furthermore, sign. changes were registered in the central amygdala, in the subcommissural organ and dorsal raphe nucleus.

Conclusions: Autoradiographic study in vitro indicates that after chronic treatment Quinapril is able to cross the blood brain barrier and suppress central ACE activity. ACE inhibition with Quinapril markedly influences vasopressin in important brain areas which are involved in central cardiovascular regulation. Therefore, central modulatory effects of ACE inhibitor may contribute to their overall therapeutic efficacy.

901-112 Attenuation of Myocardial Stunning by a Novel Nonglucocorticoid 21-Aminosteroid Inhibitor of Lipid Peroxidation

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Lipid peroxidation induced by oxygen free radicals has been implicated in myocardial dysfunction during reperfusion. The effect of a new 21-aminosteroid (Lazaroid, U74389G) that inhibits lipid peroxidation was studied in isolated, isovolumic rat hearts subjected to 20 min of normothermic ischemia and subsequent repefusion for 30 min. Male Sprague-Dawley rats (350–400 g) were randomized into three groups. Group 1 (Control; n = 13) received vehicle before sacrifice and drug-free reperfusion, group 2 (Pretreatment; n = 11) received 6 mg/kg (iv) U74389G 30 min prior to sacrifice, and group 3 (Reperfusion; n = 11) received 5 μM U74389G in the reperfusion solution. LV developed pressure (LVDP) and end-diastolic pressure (LVEDP) were measured; maximum +dP/dt and the time constant of relaxation, Tau (τ), were calculated.

	LVDP (mmHg)	+dP/dt (mmHg/sec)	LVEDP (mmHg)	Tau (msec)
Control group				
Baseline	127 ± 6	2892 ± 127	5 ± 1	23 ± 1
30 min reperfusion	66 ± 5	1673 ± 140	30 ± 6	58 ± 9
Pretreatment group				
Baseline	122 ± 3	2893 ± 97	7 ± 1	24 ± 1
30 min reperfusion	112 ± 3**	3171 ± 159**	14 ± 3*	28 ± 3*
Reperfusion group				
Baseline	124 ± 4	2744 ± 77	5 ± 1	21 ± 1
30 min reperfusion	108 ± 5**	2785 ± 129**	14 ± 5*	32 ± 9*

*$P < 0.05$ vs. Control group, 30 min reperfusion; **$P < 0.01$ vs. Control group, 30 min reperfusion

Conclusion: Whether administered before ischemia or during reperfusion in this model, U74389G attenuates the systolic and diastolic dysfunction of myocardial stunning, most likely by protecting the lipid component of cell membranes from peroxidation by oxygen-derived metabolites.

901-113 Endothelin Receptor Antagonists in a Beagle Model of Pulmonary Hypertension: Contribution to Possible Potential Therapy?

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The idealvasodilator for pulmonary hypertension (PH) would decrease pulmonary arterial pressure with minimal systemic hypotension. The present study was undertaken to investigate the pharmacologic effect of endothelin receptor antagonists on cardiopulmonary hemodynamics in an animal model of PH. We recently developed a beagle model of PH which allows accurate determination of cardiopulmonary hemodynamics and which is associated with elevated plasma endothelin-1 concentrations similar to PH in humans. Twelve beagles (PH, n = 6; and Control, n = 6) were studied during baseline conditions and during right atrial infusion of FR139317 (the ETA receptor antagonist), RES-701-1 (the ETB receptor antagonist), nitroglycerin, and prostaglandin E1. PH was induced in experimental animals 8 weeks after an injection of 3 mg/kg dehydromonocrotaline. The table showed hemodynamic values of PH beagles at baseline and during drug infusion. FR139317 lowered pulmonary and systemic arterial pressure both in pulmonary hypertensive and control animals, with a significantly greater effect on pulmonary arterial pressure in pulmonary hypertensive animals. RES-701-1 increased pulmonary arterial pressure only in PH. Nitroglycerin depressed pulmonary and systemic arterial tone equally well in controls and animals with PH. Prostaglandin E1 produced a greater decrease in systemic arterial pressure in pulmonary hypertensive than in normal animals, despite same effect on pulmonary arterial pressure in both.

	Baseline	FR139317 200 μg/kg/min	RES-701-1 100 μg/kg/min	Nitroglycerin 10 μg/kg/min	Plastaglandin E1 0.4 μg/kg/min
MSAP (mmHg)	106 ± 5	101 ± 7	109 ± 6	87 ± 6*	93 ± 7*
MPAP (mmHg)	33.2 ± 5.9	26.8 ± 3.7*	36.2 ± 6.4	27.0 ± 5.1*	27.8 ± 4.1*
SVR (dynes/s/cm^5)	4685 ± 439	4581 ± 608	4771 ± 597	3767 ± 229*	3718 ± 120*
PVR (dynes/s/cm^5)	1237 ± 441	867 ± 164*	1319 ± 299	856 ± 207*	870 ± 243*

* Significant difference between baseline and drug infusions at $P < 0.05$ levels. MSAP: mean systemic arterial pressure, MPAP: mean pulmonary arterial pressure, SVR: systemic vascular resistance, PVR: pulmonary vascular resistance

Conclusions: ETA receptor antagonists decrease pulmonary arterial pressure in a beagle model and therefore may be clinically useful for therapy of pulmonary hypertension.

PHARMACOLOGY — CLINICAL

901-114 Women Have a Higher Response Rate than Men to the Antihypertensive Calcium Channel Blocker Amlodipine

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There is a lack of data on gender difference in response to the newer antihypertensive medicines. The Amlodipine Cardiovascular Community Trial was designed to determine the blood pressure (BP) response of patient subgroups with mild-moderate hypertension to amlodipine besylate monotherapy (5–10 mg/day). After a 2 week placebo phase, patients received amlodipine for a 4 week efficacy/titration phase followed by a 12 week maintenance phase. Goal BP was defined as a decrease in diastolic BP by 10 mmHg or more *plus* a diastolic BP of less than 90 mmHg. Baseline systolic BP in mmHg was 153 ± 16 and 155 ± 16 and diastolic BP 101 ± 4 and 100 ± 4 for males (n = 702) and females (n = 382), respectively. Decreases in BP at 4 weeks were greater in females than males for both systolic (−19 vs −15 mmHg, $p < 0.0001$) and diastolic BP (−14 vs −12 mmHg, $p < 0.0001$). Results were maintained at 12 weeks. Ninety-one percent of females achieved goal BP compared to 83% of men ($p = 0.001$). The greater response to amlodipine by women remained significant after adjusting for: age, weight, dose (mg/kg), baseline BP, and drug compliance (99% in both women and men). There was no difference in decrease in systolic and diastolic BP for women on hormone replacement (−18 and −14 mmHg) versus those not on hormone replacement (−19 and −14 mmHg). Thus, hormone replacement in women did not account for the gender difference in BP response. Women reported edema